

Mechanical behaviour of degradable phosphate glass fibres and composites—a review

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Biomedical Materials



PAPER

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OPEN ACCESS

RECEIVED
8 June 2015

REVISED
19 August 2015

ACCEPTED FOR PUBLICATION
20 August 2015

PUBLISHED
23 December 2015

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Keywords: composite, bioactive, bioglass, polymer, phosphate glass, bone

Abstract

Biodegradable materials are potentially an advantageous alternative to the traditional metallic fracture fixation devices used in the reconstruction of bone tissue defects. This is due to the occurrence of stress shielding in the surrounding bone tissue that arises from the absence of mechanical stimulus to the regenerating bone due to the mismatch between the elastic modulus of bone and the metal implant. However although degradable polymers may alleviate such issues, these inert materials possess insufficient mechanical properties to be considered as a suitable alternative to current metallic devices at sites of sufficient mechanical loading.

Phosphate based glasses are an advantageous group of materials for tissue regenerative applications due to their ability to completely degrade *in vivo* at highly controllable rates based on the specific glass composition. Furthermore the release of the glass's constituent ions can evoke a therapeutic stimulus *in vivo* (i.e. osteoinduction) whilst also generating a bioactive response. The processing of these materials into fibres subsequently allows them to act as reinforcing agents in degradable polymers to simultaneously increase its mechanical properties and enhance its *in vivo* response.

However despite the various review articles relating to the compositional influences of different phosphate glass systems, there has been limited work summarising the mechanical properties of different phosphate based glass fibres and their subsequent incorporation as a reinforcing agent in degradable composite materials. As a result, this review article examines the compositional influences behind the development of different phosphate based glass fibre compositions intended as composite reinforcing agents along with an analysis of different potential composite configurations. This includes variations in the fibre content, matrix material and fibre architecture as well as other novel composites designs.

1. Introduction

Resorbable implant devices are potentially an advantageous replacement for traditional load-bearing metal implants in bone fracture fixation [1]. This is due to their ability to reduce the occurrence of stress-shielding at load bearing sites that arises from the mismatch between the elastic modulus of bone and the metal implant (table 1). The absence of mechanical stimulus by the metal implant can lead to osteopenia in the surrounding bone tissue (a reduction in the bone mineral density) which can cause bone weakening, localised bone atrophy and possible bone fracture after implant removal. Furthermore, the permanent nature of most metals also makes them susceptible to

long term complications such as wear, migration or late foreign body reactions as well as obscuring radiographs [1–5].

Thus, the use of resorbable materials that gradually degrade over time is considered by Hench [6] to be the optimal solution. Such implant devices may progressively transfer mechanical loading back to the regenerating bone which, being a dynamic tissue, is mechanostimulated to remodel according to the applied stresses [6–8]. However due to the generally poor mechanical properties of resorbable polymers (table 1) [2, 3, 9–13], the addition of a mechanically reinforcing phase is necessary to produce degradable composites suitable for substituting with metallic fracture fixation devices. These composites rely on the homogenous

Table 1. Comparison of mechanical properties human bone tissue, clinically used metals and degradable polymers used in biomedical composites [data from Kokubo *et al* (2003) [9]; Yaszemski *et al* (2003) [2], Mow and Huiskes (2005) [3], Eglin and Alini (2008) [10], Auras *et al* (2011) [13], Sin *et al* 2012 [12], Sultana (2012) [11]].

Material	Flexural strength /MPa	Elastic modulus /GPa
Cortical bone	50–150	7–30
Cancellous bone	10–20	0.05–0.5
Commercially pure titanium (CPTi) (ASTM F67)	Minimum 485	110
316L Stainless steel (ASTM F138)	Minimum 792	190
Poly-L-lactic acid (PLLA)	50–120	2.7
Poly-DL-lactic acid (PDLLA)	29–90	1.9

distribution of a high modulus (E_f), but brittle, reinforcing filler within a continuous ductile low modulus (E_m) thermoplastic matrix phase, with both the filler and matrix being biodegradable. The incorporation of the filler typically leads to increases in the elastic modulus and strength, but loss in ductility as the filler content is increased. This increase in mechanical properties is due to the transfer of externally applied stresses through the matrix to the high modulus reinforcing filler via the filler-matrix interface [14–16].

Accordingly, composite materials incorporating high modulus phosphate glass fibres (PGFs) in a degradable polymer matrix such as polylactic acid (PLA) or polycaprolactone (PCL) have been developed as potential resorbable fracture fixation devices (i.e. pins, plates and screws) [17–20]. This choice is due to the mechanical reinforcement provided by the PGFs that can also increase *in vivo* bioactivity and/or osteoinductivity via the release of ionic species into the surrounding extracellular media as the PGF degrades. Additionally, by tailoring the glass composition, specific stimulatory ions can be released into the media to evoke a desired *in vivo* response or provide a means of preventing bacterial infection at the treatment site [6, 21–23].

Furthermore, this compositional flexibility also allows for the design of PGF composites with degradation rates customised for an anatomical site or tissue to provide a specific rate of load transfer to the regenerating bone [24]. As a result, various studies have been carried out to characterise the applicability of different PGF compositions as composite reinforcing agents as well as different composite configurations (i.e. fibre volume fraction, filler architecture, matrix materials etc.). These studies aim to produce composite materials with mechanical properties similar to cortical bone and with appropriate degradation rates that would be ideally matched to the rate of tissue regeneration. Authors such as Pietrzak and Eppley [25] have suggested that degradable orthopaedic devices should retain at least 80% of their mechanical properties after six to eight weeks degradation.

Yet despite the available in-depth review articles/chapters regarding the structure, composi-

tional influences and technological applications of phosphate glasses [22, 23, 26–28], limited work has considered the mechanical properties of the various PGF compositions as well as the resulting PGF containing composite materials. Accordingly this review examines the compositional and composite configurations investigated and their related mechanical/degenerative properties relevant to the development of PGF composites as fracture fixation devices. However, given the previous review articles [22, 23, 26–28] outlining the general chemistry, structure and compositional influences of bulk phosphate glasses, basic descriptions of these features are omitted. Similarly the *in vitro* biocompatibility results are not considered in detail and the *in vivo* responses to these materials have been ignored.

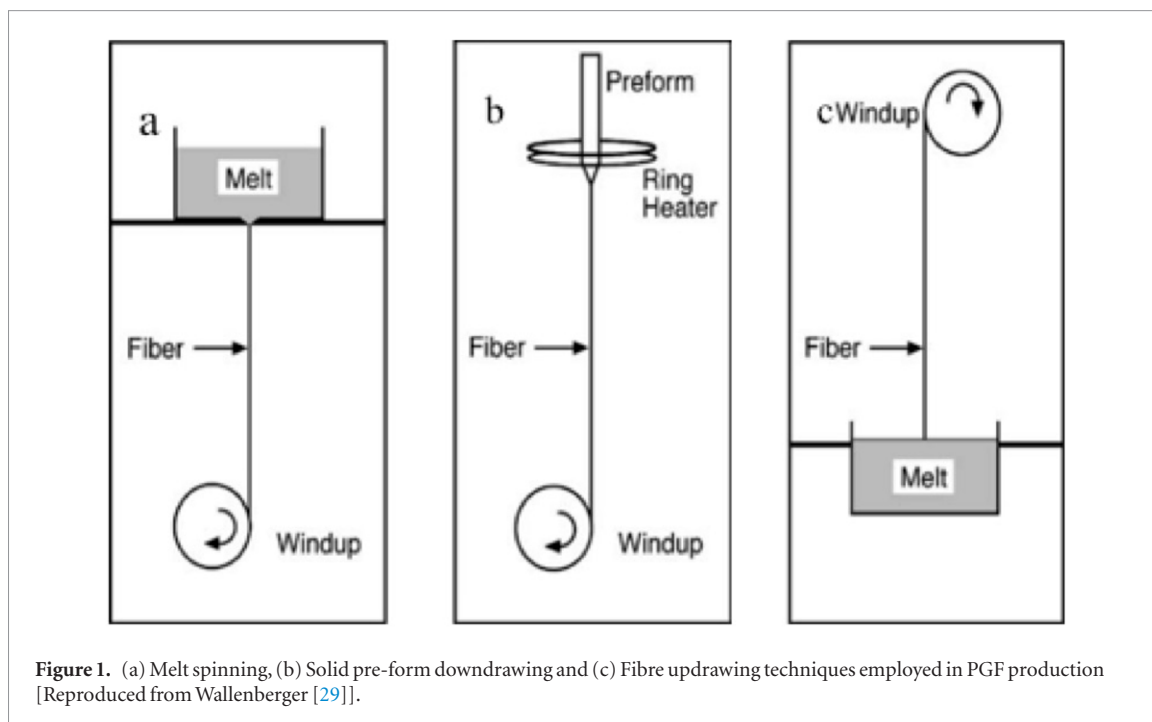
2. Phosphate glass fibres

2.1. Fibre manufacture

Continuous PGFs have conventionally been manufactured from a melt spinning technique where droplets are drawn down directly through an array of nozzles from a temperature adjusted glass melt under the influence of gravity and hydrostatic pressure. These drops are then drawn by mechanical tension and collected around a rotating drum (figure 1(a)). The glass fibre diameter and fibre-to-fibre spacing in the resulting fibre tow can be controlled by altering the manufacturing conditions such as the glass melt viscosity, hydrostatic pressure, bushing nozzle diameter and drum speed. Although other methods such as downdrawing from solid preforms and updrawing from a viscous melt have also been developed for fibre production (figures 1(b) and (c)), these have typically suffered from lower efficiencies than melt spinning techniques and are rarely used to manufacture bioglass fibres [22, 28–30].

For PGF reinforced degradable polymer composites, typically fibre diameters of $\approx 20\ \mu\text{m}$ have been used [31–35] similar to the 10–20 μm fibre diameters found in commercially available fibre reinforced composites. This is due to the high aspect ratio (i.e. fibre length-to-diameter ratio) with the large surface area per unit volume maximising stress transfer and thus reinforcement for the composite [36–39].

However, not all glass compositions are suitable for fibre formation. The ability to form fibres is dependent upon achieving a glass melt of suitable viscosity (typically between 10^3 – 10^6 Pa·s) without the glass crystallising. Crystalline fibres have poor processability (i.e. fibre forming) along with reduced mechanical properties and limited bioactivity. Furthermore the ability to draw fibres is typically dependent upon the potential to draw the glass structure into long chains of phosphate groups with bond strengths sufficient enough to withstand the stresses incurred during fibre drawing. Accordingly it is generally considered that PGFs can be more easily manufactured from meta- (50 mol%



P_2O_5) and ultraphosphate (>50 mol% P_2O_5) compositions with modifier oxides of a high charge-to-size ratio that may also be able to act as network formers (known as intermediate oxides). These compositional features will also have an effect on the glass melt viscosity with the entanglement of the long chain Q^2 chains/ring type structures increasing the melt viscosity and subsequently impeding the reorganisation of the melt into a crystalline state [22, 24].

Given these variables, the ease of fibrillation is commonly described by the glass compositions processing window (PW) that is indicative of the glass's thermal stability (i.e. its processability). The PW is defined as the temperature range between the glass transition temperature (T_g) and the crystallisation onset temperature (T_{oc}) with values exceeding 100°C preferred for fibre drawing [22]. However, the more relevant descriptor of how easy a fibre is to draw is the temperature difference between the drawing point temperature (T_{DP}) and the liquidus temperature (T_L) with fibre production extremely difficult when T_L is equal to or greater than T_{DP} .

2.2. Fibre tensile properties

The tensile properties of phosphate glass fibres typically are tested according to BS ISO 1156 with the resulting tensile data used to determine the tensile modulus and strength of the fibres [40]. However, given that the strength of a glass or brittle ceramic is generally dependent upon its fracture toughness (K_{IC}) and critical flaw size (a), a determination of its mechanical performance requires a statistical evaluation of the flaw population. Accordingly, Weibull distribution statistics have commonly been used to characterise the statistical variation in the fracture strength of PGFs and is based on the 'weakest link theory'—where the most significant flaw will control the overall strength of a material [36, 41, 42].

The Weibull analysis is performed by calculating the Weibull modulus (m), which reflects the tensile strength distribution of a sample set. As m increases, the range of tensile strengths become narrower and the fibres mechanical properties become more predictable. For ceramics, m values typically range from 2 to 15 whilst commercial grade glass fibres possess m values from 10 to 30 [36, 42, 43]. Additionally, a normalising stress (σ_0) is also determined from the Weibull analysis and is defined by Weibull [43] as the 'stress at which 63.2% of the tested fibres had failed' or alternatively 'the most probable strength expected from a fibre of gauge length L_0 ' by Hull and Clyne [14].

2.3. Bulk versus fibre properties

Owing to differences in their thermal and mechanical histories during manufacturing, the structure and mechanical properties of PGFs can deviate significantly from the identical PG bulk composition. This is due to the mechanical drawing stress and rapid quenching (10^{-2} – 10^{-3} s) commonly experienced during fibre manufacturing that installs a degree of molecular chain alignment in the PGF structure. The frozen-in anisotropy of the P-O-P phosphate chain network parallel to the fibre's long axis consequently results in an increased tensile modulus compared to the equivalent bulk artefact with the practical tensile strength considered to be reflective of the fibre's surface quality [22, 28, 44, 45]. Additionally, besides compositional influences, the mechanical properties of a glass fibre are also considered by Pähler and Brückner [46] to be strongly influenced by the cooling rate and drawing stress experienced during manufacturing (due to its effects on the fibres structural anisotropy) [22, 24, 28, 44, 45].

Given that the mechanical and dissolution properties of PGFs share the same compositional dependencies as phosphate glass (PG) monoliths, the tailoring

of PGF materials can be achieved in the same manner as conducted with bulk glass samples. Thus tailoring of the fibre's dissolution rate (D_r), tensile modulus and inherent tensile strength can be achieved through the appropriate choice of specific cationic species and compositional concentrations due to their effect on the average bond strengths, degree of ionic cross-linking and phosphate chain length [24, 47]. Yet despite following the same dissolution mechanisms as bulk monoliths, PGFs typically lose mass faster than the equivalent monolith due to the larger surface area to volume ratios during dissolution.

2.4. Compositional investigations

The ability to manufacture PGFs and their resulting material properties are strongly dependent upon the selection and quantities of the compositional components in the glass formulation. Glasses are made of a number of metal oxides and can range from a simple binary composition through to more complex ternary, quaternary and quinary glass systems as the number of oxides increases.

The development and systematic characterisation of Ø8–40 μm fibres based on a ternary P_2O_5 –CaO– Na_2O glass system was examined by Ahmed *et al* [47] to identify compositional dependencies on PGF processability. The analysis of ultra- (55 mol% P_2O_5), meta- (50 mol% P_2O_5), and polyphosphate (45 mol% P_2O_5) compositions with varying CaO concentrations showed that fibres could not be manufactured from these ternary polyphosphate glasses. This was attributed to the short-chained network structure created from the comparatively low P_2O_5 content that, upon heating, immediately generated melts with too low a viscosity for fibre manufacture. This is due to the liquidus temperature being too close to the drawing point temperature. Furthermore, these glasses have a tendency to crystallise once below T_L . Compositional influences from the substitution of Na_2O with increasing amounts of CaO showed the expected increase in glass T_g and decrease in PGF D_r from $\approx 7 \text{ mg cm}^{-2} \text{ h}^{-1}$ (P_2O_5)₅₀–(CaO)₃₀–(Na_2O)₂₀ to $\approx 1 \text{ mg cm}^{-2} \text{ h}^{-1}$ (P_2O_5)₅₀–(CaO)₄₀–(Na_2O)₁₀, confirming the same compositionally dependant properties for the PGFs as previously reported for the equivalent glass monolith samples by Uo *et al* [48] and Franks *et al* [49]. Further examination on the dependence of PGF manufacturing showed the expected decrease in fibre diameter with increasing pulling speed (i.e. drum speed) whilst no correlation was found between the glass composition and the fibre diameter. Increase in drum speeds were also found to coincide with an increase in PGF mass loss as a result of the reduced fibre diameter and subsequently increased sample surface area to volume ratio [47].

Owing to the limitations of the previous ternary composition, further flexibility to the PGF properties has been investigated for a set of quaternary compositions via the incorporation of Fe_2O_3 [41, 50–52]. The characterisation of metaphosphate fibres in the

(P_2O_5)–(CaO)–(Na_2O)–(Fe_2O_3) system by Ahmed *et al* [51] found a decrease in PGF D_r with increasing Fe_2O_3 content (mol%) that ranged from $\approx 20 \text{ mg cm}^{-2} \text{ h}^{-1}$ for (P_2O_5)₅₀–(CaO)₄₀–(Na_2O)₉–(Fe_2O_3)₁ to $\approx 3.5 \text{ mg cm}^{-2} \text{ h}^{-1}$ for (P_2O_5)₅₀–(CaO)₄₀–(Na_2O)₅–(Fe_2O_3)₅. This decrease in D_r was attributed to the increased bond strength and ionic cross-links between the phosphate chains as the Fe_2O_3 content increased. The reduced D_r was also coupled with an increased attachment and differentiation of mesenchymal progenitor cells (MPC) on fibre compositions containing 4–5 mol% Fe_2O_3 [51]. This data echoed similar biocompatibility results found by Bitar *et al* [52] for a (P_2O_5)₅₀–(CaO)₄₆–(Na_2O)_(4-x)–(Fe_2O_3)_x (mol%) system when cultured with human craniofacial osteoblasts over x: 0, 1, 2, or 3 mol% compositions [52]. A comparison between PGF D_r ($\approx 3.5 \text{ mg cm}^{-2} \text{ h}^{-1}$) and bulk samples ($> 5 \times 10^{-4} \text{ mg cm}^{-2} \text{ h}^{-1}$) over the same (P_2O_5)₅₀–(CaO)₄₀–(Na_2O)₅–(Fe_2O_3)₅ composition also agreed with the previously observed large difference in solubility due to surface area effects [51]. Meanwhile, mechanical testing of (P_2O_5)₅₀–(CaO)₄₀–(Na_2O)₅–(Fe_2O_3)₅ (mol%) fibres by Ahmed *et al* [41] found a tensile strength (σ_f) of 456 MPa and tensile modulus (E_f) of 51.5 GPa coupled with a Weibull modulus (m) of 3.37 and a normalising stress (σ_0) of 508 MPa. In contrast, a simpler, binary (P_2O_5)₅₀–(CaO)₅₀ fibre system was investigated by Ahmed *et al* [32] who recorded the fibre σ_f and E_f as 474 MPa and 44 GPa respectively with a Weibull modulus of 4.07 and normalising stress of 524 MPa.

Fibre dissolution studies by Patel and Knowles [53] examined the effects of SiO_2 addition into this system to produce a more complex quinary composition. This was intended to accelerate the fibre D_r without the associated pH drop produced by the formation of phosphoric acid in the dissolution media (via the release of phosphate ionic species). Testing of different (P_2O_5)₅₀–(CaO)₃₀–(Na_2O)_(15-x)–(Fe_2O_3)₅–(SiO_2)_x (x: 0, 1, 3, or 5 mol%) fibres confirmed the increased D_r in glasses containing 5 mol% SiO_2 whilst it appeared that the pH changes produced by PGF dissolution were suitably buffered (i.e. maintained within a biocompatible range) when degraded in cell culture media. These results were coupled with a general trend of increasing the glass transition and crystallisation temperatures as the SiO_2 concentration was increased with the attachment of MG63 human osteosarcoma cells to all compositions after 24 h of culture. However no mechanical data was reported for these compositions [53].

Alternatively the incorporation of MgO into the quaternary system (P_2O_5)–(CaO)–(Na_2O)–(Fe_2O_3) studied by Ahmed *et al* [51] was examined by Cozien-Cazuc *et al* [54] for a batch of Ø $\approx 15 \mu\text{m}$ (P_2O_5)₄₀–(Na_2O)₂₀–(CaO)₁₆–(MgO)₂₄ (mol%) fibres during one week's degradation in distilled water at 37 °C. This was to examine the effects of aqueous aging on the fibres initial mechanical properties ($\sigma_f = 484 \pm 153 \text{ MPa}$, $E_f = 44.0 \pm 4.8 \text{ GPa}$, $m = 3.6$, $\sigma_0 = 538$). The results showed that the tensile strength decreased over the

immersion period with surface cracking of the fibres, coupled with an increase to the Weibull modulus ($m = 5.2$) due to the reduced variation in tensile strengths ($\sigma_f = 323 \pm 83$ MPa). However, as the glass's intrinsic structure remained unchanged, the tensile modulus remained constant [54].

The same study also examined the effects of annealing the PGFs with regards to improving their durability [54]. Compared to the as-made fibres, the annealing process reduced the initial tensile strength ($\sigma_f = 288 \pm 51$ MPa) whilst increasing the tensile modulus ($E_f = 52.0 \pm 4.7$ GPa) and Weibull modulus (6.0). The change in tensile modulus was attributed to structural changes whilst the decreased tensile strength was related to an increase in fibre surface flaws due to ambient moisture attacking the fibre surfaces during the annealing process. However, during immersion, the tensile strength was seen to recover after seven days of dissolution ($\sigma_f = 459 \pm 136$ MPa) that was attributed to the removal of an outer tensile layer (and its associated flaws) on the fibre surface. Furthermore subsequent studies by Cozien-Cazuc *et al* [45] with this PGF composition demonstrated a reduced D_r from 1.2×10^{-2} mg cm $^{-2}$ h $^{-1}$ to 6.7×10^{-3} mg cm $^{-2}$ h $^{-1}$ from the annealing process due to the relaxation of the phosphate chains into a more stable configuration.

The addition of Fe $_2$ O $_3$ into this system was investigated by Felfel *et al* [55] for a quinary (P $_2$ O $_5$) $_{40}$ –(CaO) $_{16}$ –(Na $_2$ O) $_{16}$ –(MgO) $_{24}$ –(Fe $_2$ O $_3$) $_4$ composition of $\varnothing \approx 15$ μ m fibres. The substitution of Na $_2$ O with Fe $_2$ O $_3$ (compared to the fibres studied by Cozien-Cazuc *et al*) produced fibres with an increased tensile modulus (73 ± 10 GPa), Weibull modulus (6.3) and decreased D_r (3×10^{-3} mg cm $^{-2}$ h $^{-1}$) that followed the expected trends from the previous results obtained with similar Fe $_2$ O $_3$ incorporating compositions. The addition of Fe $_2$ O $_4$ was also seen to decrease the tensile strength ($\sigma_f = 318 \pm 46$ MPa) and the normalising stress to 340 MPa compared to the composition examined by Cozien-Cazuc *et al* [45, 54].

Stemming from this, a range of (P $_2$ O $_5$) $_{40}$ –(MgO) $_{24}$ –(CaO) $_{16}$ –(Na $_2$ O) $_{(20-x)}$ –(Fe $_2$ O $_3$) $_x$ (x : 0, 2, or 4 mol%) and (P $_2$ O $_5$) $_{(50-y)}$ –(MgO) $_{24}$ –(CaO) $_{16}$ –(Na $_2$ O) $_y$ –(Fe $_2$ O $_3$) $_4$ (y : 0, 5, or 7.5 mol%) PGFs were investigated by Hasan *et al* [34]. The increased P $_2$ O $_5$ content was found to ease fibre manufacturing whilst producing an increase in fibre tensile strength from 370 ± 8 MPa (45 mol% P $_2$ O $_5$) to 456 ± 144 MPa (50 mol% P $_2$ O $_5$). This was coupled with changes to the tensile modulus that ranged from 50–75 GPa. Decreases to the PGF D_r were also found as the phosphate content increased due to the increased time required for longer phosphate chains to hydrate before they dissociated from the glass into the media. However, even the most durable (P $_2$ O $_5$) $_{50}$ –(CaO) $_{16}$ –(MgO) $_{24}$ –(Na $_2$ O) $_6$ –(Fe $_2$ O $_3$) $_4$ (mol%) PGF composition (1.8×10^{-3} mg cm $^{-2}$ h $^{-1}$) was found to be below the suggested PGF dissolution rate (2×10^{-4} mg cm $^{-2}$ h $^{-1}$) required for bone repair applications and composite reinforcement [34].

Haque *et al* [35] examined the mechanical property variations between different fibre batches of the same (P $_2$ O $_5$) $_{40}$ –(MgO) $_{24}$ –(CaO) $_{16}$ –(Na $_2$ O) $_{16}$ –(Fe $_2$ O $_3$) $_4$ (mol%) composition previously studied by Hasan *et al* [56]. They showed that inter-sample variations existed in the tensile strengths and tensile moduli ($\sigma_f = 251 \pm 14, 321 \pm 22, 310 \pm 12$ MPa and $E_f = 54 \pm 2, 74 \pm 2, 62 \pm 2$ GPa respectively) between batches that was attributed to variations in the fibre diameter and surface damage. This result agreed with the variations in fibre diameter previously discussed by Kobayashi *et al* [57] where the fibre diameter was found to decrease as the production time increased (due to the decreasing volume of the glass melt and subsequent changes to the hydrostatic pressure). The data collected by Haque *et al* [35] found these fibres to have a D_r of 2.9×10^{-3} mg cm $^{-2}$ h $^{-1}$ but, in contrast to the results of Cozien-Cazuc *et al* [54], no change in the mechanical properties of these fibres was recorded over the dissolution period [35, 54].

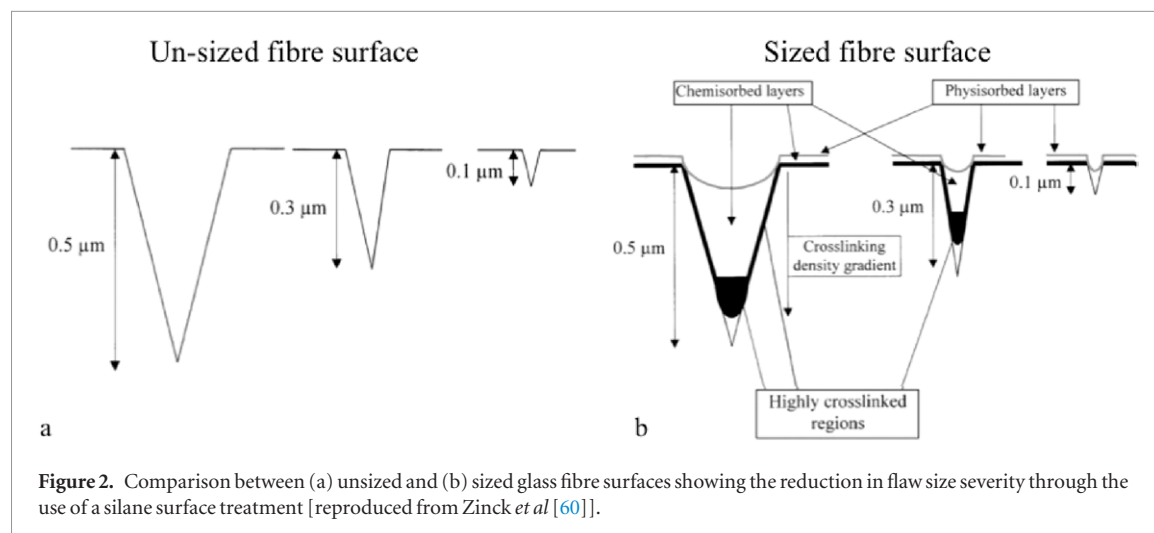
Similarly, a (P $_2$ O $_5$)–(Na $_2$ O)–(MgO)–(CaO)–(B $_2$ O $_3$) system was examined by Sharmin *et al* [24] for meta- (50 mol% P $_2$ O $_5$) and polyphosphate (40, 45 mol% P $_2$ O $_5$) glass fibre compositions with increasing concentrations of B $_2$ O $_3$ (0, 5, 10 mol%). Boron oxide was selected as a modifier based on previous data [58] that found B $_2$ O $_3$ to reduce the D_r whilst improving the glass's thermal stability and *in vivo* response. These effects were due to the increased bond strengths as well as the ability of B $_2$ O $_3$ to act easily as either a modifier oxide or a network former (i.e. intermediate oxide) [24, 58]. The investigation was aimed at assessing the processability, mechanical and degenerative properties of as-made and annealed fibres with different compositions due to the improved biocompatibility found from fibre compositions with <50 mol% P $_2$ O $_5$.

The results of this study found that the ease of fibre manufacturing increased as the P $_2$ O $_5$ and/or the B $_2$ O $_3$ content increased due to the resulting changes to the structural bond strengths and network dimensionality (i.e. increased network chain length). For as-made fibres, this ease in fibre manufacturing was coupled with increases to the tensile strength (σ_f) and normalising stress (σ_0) with Weibull modulus (m) values ranging from 7.7 to 10.5. It is worth noting that the tensile strength achieved from the (P $_2$ O $_5$) $_{45}$ –(CaO) $_{16}$ –(Na $_2$ O) $_5$ –(MgO) $_{24}$ –(B $_2$ O $_3$) $_{10}$ composition (1200 ± 146 MPa) was higher than any previous set of ≤ 25 μ m diameter phosphate glass fibres tested as potential composite reinforcements [24].

The fibre tensile modulus (E_f) was also found to change with alterations to the P $_2$ O $_5$ and B $_2$ O $_3$ content with increases to E_f found through the incorporation of 5 mol% B $_2$ O $_3$ into 40, 45 or 50 mol% P $_2$ O $_5$ glass compositions ($E_f = 59.2 \pm 3, 59.6 \pm 2$ and 61.4 ± 3 GPa respectively) [24]. In contrast, a decrease in tensile modulus was found as the P $_2$ O $_5$ increased from 40 to 45 mol% ($E_f = 56.5 \pm 2, 53.4 \pm 1$ GPa respectively). However further increases in the P $_2$ O $_5$ content from 45

Table 2. Comparison of initial PGF tensile strength and tensile modulus and after degradation along with the correlating dissolution rate [data from Sharmin *et al* (2014) [24]].

Composition (mol%)	σ_f (MPa)		E_f (GPa)		
	T_0	$T_{28\text{ d}}$	T_0	$T_{28\text{ d}}$	
$(\text{P}_2\text{O}_5)_{45}-(\text{CaO})_{16}-(\text{Na}_2\text{O})_{15}-(\text{MgO})_{24}$	530 ± 67	$\approx 200^a$	53.4 ± 2	52.3 ± 2^a	2.53×10^{-3}
$(\text{P}_2\text{O}_5)_{45}-(\text{CaO})_{16}-(\text{Na}_2\text{O})_{10}-(\text{MgO})_{24}-(\text{B}_2\text{O}_3)_5$ (Non-annealed)	1050 ± 165	710 ± 134	59.1 ± 2	55.4 ± 5	1.97×10^{-3}
$(\text{P}_2\text{O}_5)_{45}-(\text{CaO})_{16}-(\text{Na}_2\text{O})_{10}-(\text{MgO})_{24}-(\text{B}_2\text{O}_3)_5$ (Annealed)	≈ 350	≈ 600	63.8 ± 2	66.5 ± 8	1.25×10^{-3}

^a Measured after 7 d of degradation.

to 50 mol% or the incorporation of 10 mol% B_2O_3 into the glass composition provided no statistically significant changes in E_f [24]. The subsequent dissolution of these fibres over 28 d in Phosphate Buffered Saline (PBS) at 37 °C found a reduction in tensile strengths for all compositions but also that faster decreases were found in the B_2O_3 -free fibres compared to the B_2O_3 containing compositions. This result was due to the reduced PGF dissolution rate in the B_2O_3 containing glasses with the post dissolution weakness of the B_2O_3 -free fibres after seven days immersion preventing any mechanical testing after longer immersion periods (table 2). Meanwhile, no significant changes in the tensile modulus were found for any of the fibre compositions during sample dissolution [24].

Due to the factors previously discussed by Cozien-Cazuc *et al* [45, 54], the annealing of these PGFs by Sharmin *et al* [24] resulted in decreases to the initial tensile strength and D_r with increases to the tensile modulus and sample density also recorded. The dissolution of these annealed fibres over 60 d in PBS at 37 °C also showed the recovery of the tensile strength with increasing immersion time. No change in the tensile modulus was recorded (table 2), agreeing with the previous results of Cozien-Cazuc *et al* [45, 54]. The subsequent changes to the fibre processability, mechanical properties and D_r were attributed to the higher chain lengths, increased ionic cross-linking and increased bond strengths from the addition of B_2O_3 which, due to its ability to act as an intermediate oxide, created hydration resistant P-O-B-O-P bonds in the backbone of the glass network [24].

Meanwhile a more complex boron incorporating glass $(\text{P}_2\text{O}_5)_{40}-(\text{B}_2\text{O}_3)_{10}-(\text{SiO}_2)_5-(\text{MgO})_5-(\text{CaO})_{20}-(\text{K}_2\text{O})_{10}-(\text{Na}_2\text{O})_{10}$ (mol%) glass composition was investigated by Zheng *et al* [59] who manufactured 30–40 μm \varnothing PGFs using melt viscosities of $10^{4.5}$ – 10^5 Pa·s. Although no mechanical or dissolution testing was performed, this composition was deemed to show potential for tissue regenerative applications due to its bioactivity and the attachment of MG63 human osteosarcoma cells after 24 h of culture [59].

2.5. Fibre modifications

In addition to the glass composition and thermal modifications (i.e. annealing) applied to PGFs, sizing agents have also been investigated to improve the interfacial bonding in the composite matrix while also introducing a degree of interfacial hydrophobicity between the composite phases. Furthermore authors such as Zinck *et al* [60, 61] and Feih *et al* [62] have demonstrated the ability of coupling agents to repair partially the fibres surface flaws through the deposition, penetration and crosslinking of the sizing agent within the surface defects (figure 2).

A direct comparison of $\varnothing \approx 22 \mu\text{m}$, $(\text{PO}_4)_{54}-(\text{CaO})_{27}-(\text{ZnO})_{12}-(\text{Fe}_2\text{O}_3)_{4.5}-(\text{NaPO}_3)_{2.5}$ fibres was conducted by Rinehart *et al* [63] who compared the effects of temperature and a tetramethoxysilane $(\text{Si}(\text{OCH}_3)_4)$ sizing agent on this PGF's D_r in PBS. As expected, an increase in temperature from 37 °C to 60 °C produced distinct increases to the fibre D_r from $6.5 \times 10^{-4} \text{ mg cm}^{-2} \text{ h}^{-1}$ to $2.5 \times 10^{-3} \text{ mg cm}^{-2} \text{ h}^{-1}$. However due to the lack of siloxane covalent bonding

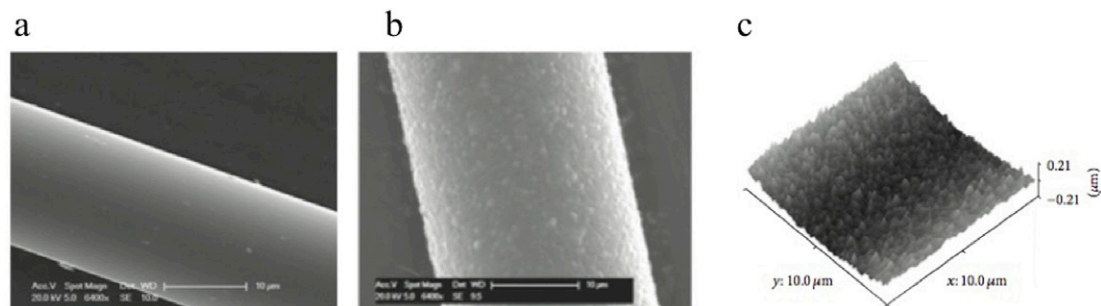


Figure 3. Comparison of PGF surfaces prior to and after the deposition of $0.8\ \mu\text{m}$ thick Mg coating showing (a) SEM of fibre surface prior to sputter coating, (b) SEM image of fibre surface with $0.8\ \mu\text{m}$ thick Mg coating and (c) AFM of a $0.8\ \mu\text{m}$ thick Mg coating after sputter coating a glass slide [reproduced from Liu *et al* [65]].

between the PGF surface and the sizing agent, the fibre D_r at 37°C was similar to ‘as made’ fibres [63]. Similar results comparing the fibre D_r were also found by Cozien-Cazuc *et al* [45] who recorded PGF D_r of $1.2 \times 10^{-2}\ \text{mg cm}^{-2}\ \text{h}^{-1}$ and $1.7 \times 10^{-2}\ \text{mg cm}^{-2}\ \text{h}^{-1}$ for as-prepared and silane treated $(\text{P}_2\text{O}_5)_{40}\text{--}(\text{CaO})_{24}\text{--}(\text{Na}_2\text{O})_{20}\text{--}(\text{MgO})_{24}$ (mol%) fibres respectively. As before, this was attributed to a lack of chemical bonding between the fibres and the 3-aminopropyltriethoxysilane (APS) coupling agent that was believed to have gone into solution upon the immersion of samples. The mechanical properties of these APS treated fibres over the same immersion period by Cozien-Cazuc *et al* [54] found that these fibres displayed a faster reduction in tensile strength in one week compared to as-prepared fibres. This was attributed to the sizing treatment process where the temperatures required to cure the coupling agent (120°C) may have increased the severity of the surface flaws in the fibres. However from these results Cozien-Cazuc *et al* [45, 54] discussed how decreases in the fibre D_r may be achieved through the use of alternative coupling agents or preparation routes. With this in mind, hexamethylene diisocyanate (HDI) and sorbitol ended PLA oligomer (SPLA) coupling agents were applied to PGFs by Hasan *et al* [64] for composite reinforcement. However no mechanical or dissolution data was provided for these fibres alone.

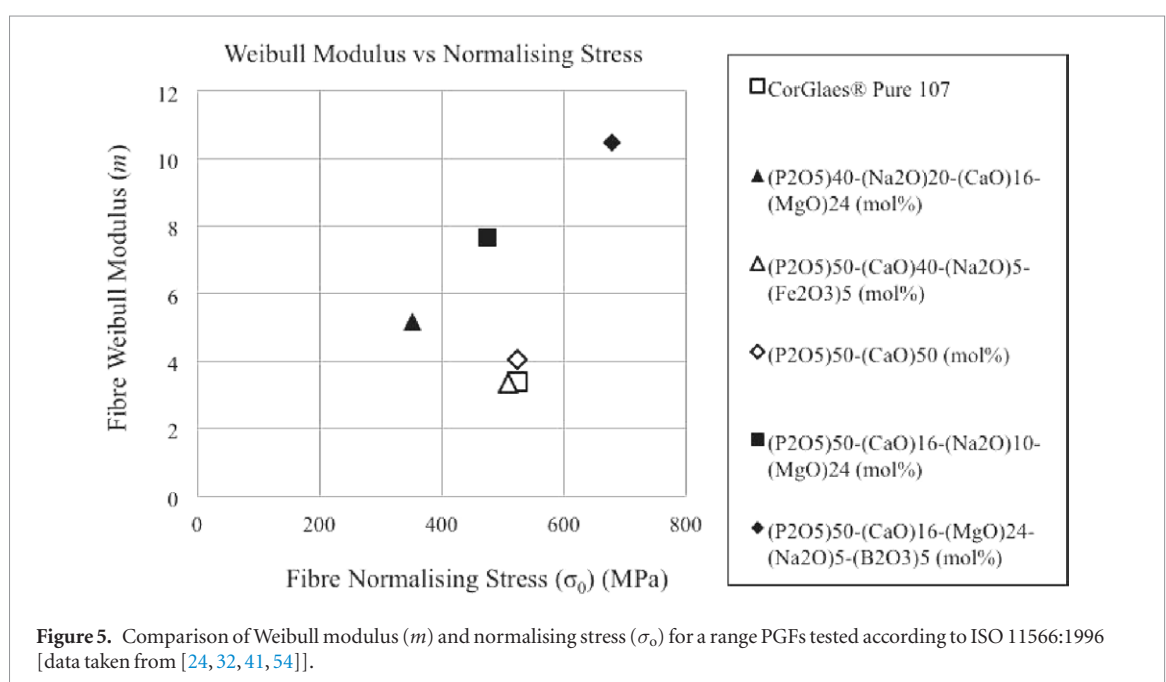
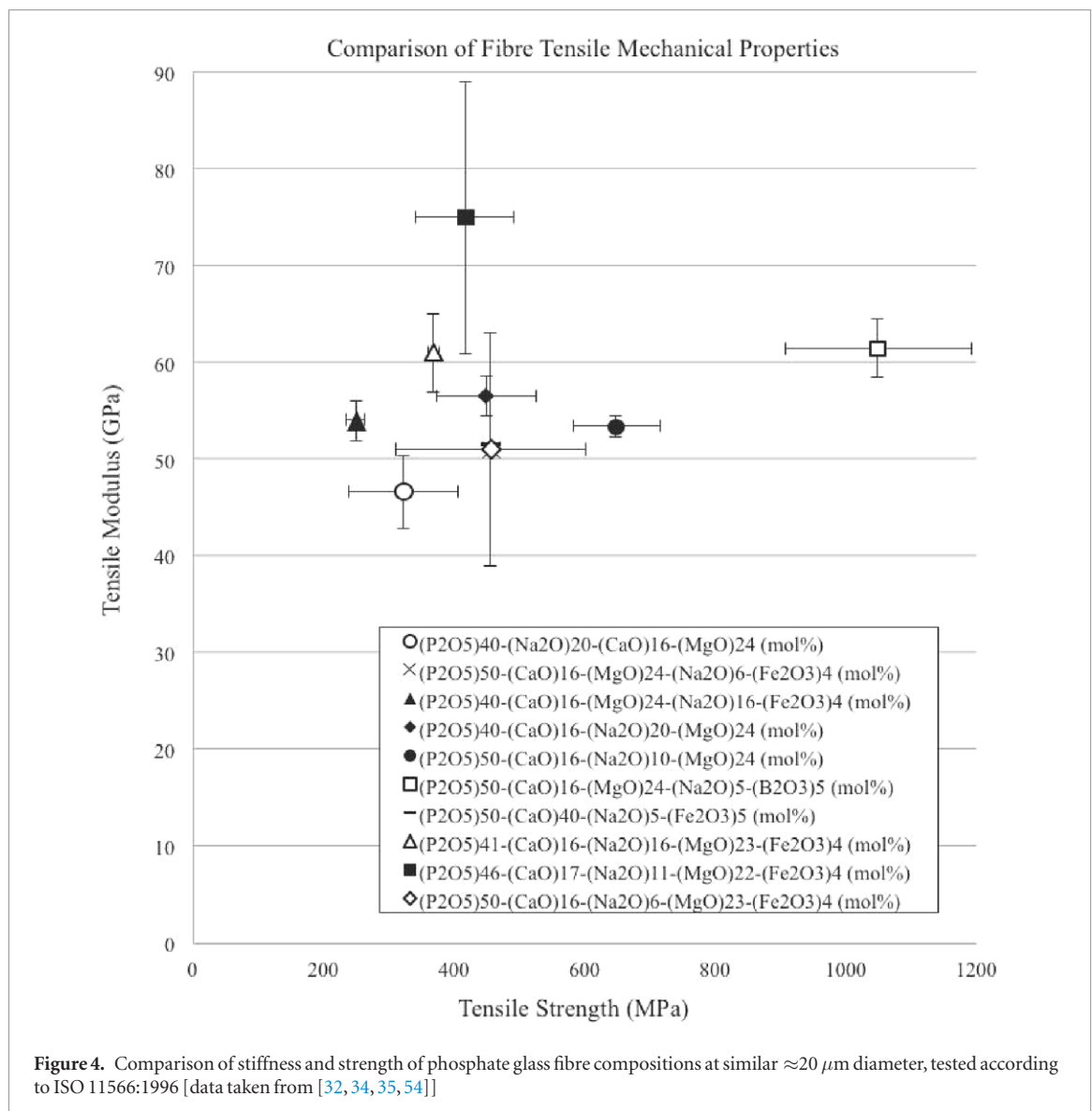
Other novel modifications, such as the deposition of a biocompatible, degradable magnesium coating onto $(\text{P}_2\text{O}_5)_{45}\text{--}(\text{CaO})_{16}\text{--}(\text{MgO})_{24}\text{--}(\text{Na}_2\text{O})_{11}\text{--}(\text{Fe}_2\text{O}_3)_4$ (mol%) fibres was investigated as a surface modification by Liu *et al* [65]. The application of this coating via a sputter coating process was intended to improve the interfacial adhesion between the fibre and matrix by increasing the mechanical interlock between each phase. Tensile testing of this fibre composition found that the tensile strength ($546 \pm 46\ \text{MPa}$) and tensile modulus ($57 \pm 1\ \text{GPa}$) decreased to $463 \pm 15\ \text{MPa}$ and $48 \pm 0.2\ \text{GPa}$ respectively after the application of a $0.8\ \mu\text{m}$ thick Mg coating (figure 3) [65]. The reduction in fibre tensile properties were also observed to increase with increasing sputter coating time, considered to be due to the creation or enlargement of existing surface flaws as the fibres were struck with Mg atoms over

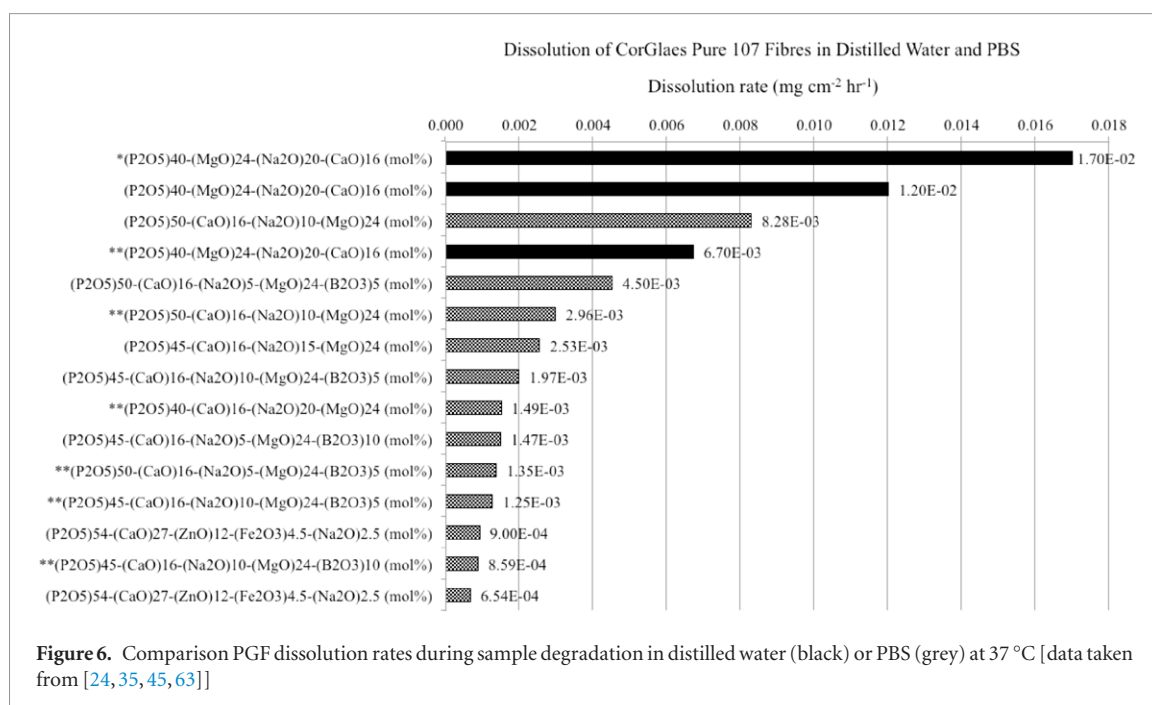
prolonged periods. Furthermore stress differentials, created by the difference in fibre and magnesium thermal expansion coefficients, were also expected to play a role in reducing the fibre mechanical properties. However no degradation studies were conducted to assess the effect of this Mg coating on the fibre dissolution behaviour [65].

2.6. Discussion of glass fibre properties

The examination of various phosphate glass fibre compositions has shown how improvements in the ease of fibre manufacturing, mechanical properties (figures 4 and 5) and reductions to the dissolution rate (D_r) (figure 6) can be achieved by tailoring the PGF composition. This includes alterations to the P_2O_5 content as well as through the incorporation and/or increases to the modifier oxides with high charge-to-size ratio cations that can increase the phosphate chain length, the degree of ionic cross-linking and network bond strength. However, the studies have also highlighted the dichotomy that can exist in PGF compositions due to the increase in ease of fibre processability with increased P_2O_5 content being offset by reduced biocompatibility (Sharmin *et al* [24]). Accordingly, compounds that can act as intermediate oxides (such as Fe_2O_3 or B_2O_3) appear to be an attractive option for developing PG compositions that can easily manufactured into fibres whilst maintaining biocompatibility [24, 51, 52].

Meanwhile mechanical testing of PGF samples showed that despite their compositionally dependent mechanical properties, the fibre’s practical tensile strength and their dependency on the sample surface quality must also be considered. Such factors have been discussed by De Diego *et al* [66] who believed that the presence of these surface flaws produces a more accurate representation of a PGF’s practical behaviour when used as a composite reinforcing agent due to the handling fibres experience during composite manufacture. Additionally, despite achieving PGFs with tensile moduli within the same range as commercial S-glass fibres ($E_f = 86.9\ \text{GPa}$) or E-glass fibres ($\sigma_f = 3450\ \text{MPa}$, $E_f = 72.4\ \text{GPa}$), typical PGF tensile strengths compared to S-glass fibres ($\sigma_f = 4300\ \text{MPa}$), or E-glass fibres





($\sigma_f = 3450 \text{ MPa}$) remain significantly lower (figure 4) [34, 35, 68]. Furthermore, the majority of the Weibull modulus (m) values also remain considerably lower than those quoted for commercial grade glass fibres ($m = 10\text{--}30$) (figure 5) [66, 67].

With regards to the data shown in figure 6, a direct comparison between the dissolution rates of different PGF samples is compromised by the differences in the surface area to volume ratios (SA:V) used by different authors ($0.15, 7.3 \text{ cm}^2 \text{ ml}^{-1}$ etc.). The influence of the PGF dissolution media ionic concentration is another important factor due to the known ionic buffering effects as reported by Franks *et al* [49] and Patel and Knowles [53]. As discussed by Mohammadi *et al* [68], the SA:V will have a significant effect on the fibre dissolution rate and any resulting autocatalytic effects from the phosphoric acid (H_3PO_4) by-product formed. Furthermore, significantly higher SA:V volume ratios would be expected at the fibre-matrix interface of a composite compared to the dissolution data quoted in figure 6. As a result, any autocatalytic effects would likely be increased if such PGF samples were used as composite reinforcement. Thus the development of fibre compositions similar to those studied by Patel and Knowles [53], which aim to maintain a neutral media pH during PGF dissolution is a promising avenue for creating suitable PGF composite reinforcing agents.

Yet despite these variations in testing and sample conditions (i.e. annealing), no PGF composition (figure 6) has yet been developed with D_r s within the desired value of $2 \times 10^{-4} \text{ mg cm}^{-2} \text{ hr}^{-1}$ that has been discussed by Hasan *et al* [69] for composite reinforcement. This data also shows that post fibre-processing effects such as annealing are suitable to reduce the fibre D_r , but at the cost of reductions in the tensile strength [24, 45, 54]. Additionally, despite the perceived interfacial benefits

of using coupling agents on the resulting composite properties, the use of APS treated PGFs has so far failed to demonstrate any significant reduction in the fibre D_r [45, 63]. However alternative methods or treatment protocols may yet provide advantageous results. With this in mind, the use of more novel methods such as those investigated by Liu *et al* [65] may also provide routes for simultaneously enhancing the fibre durability and resulting composite mechanical properties.

3. Composites overview

Composites are typically defined as materials composed of at least two physically or chemically different constituent phases separated by a distinct interface [70, 71]. The incorporation of a filler phase into a ductile matrix can increase the composite elastic modulus (E_{comp}), strength (σ_{comp}) and other mechanical properties compared to the matrix phase, but this is also coupled with a reduction in the strain at failure and toughness as the filler content is increased [72]. Furthermore, given that the densities of the two phases typically differ by a factor of 2–3 in glass reinforced polymer composites, it is important to clarify whether the filler content is being defined as volume fraction (V_f) or weight fraction (W_f), which can be overlooked by some authors.

3.1. Fibrous composite precursors, manufacturing and design

The mechanical properties of a composite are dependent upon the properties of each constituent phase, filler geometry and quality of the fibre-matrix interface (e.g. via coupling agents). Accordingly, substantial variations in the mechanical properties of the resulting composites (typically measured according to BS EN ISO 14125:1998) [73] can be achieved through

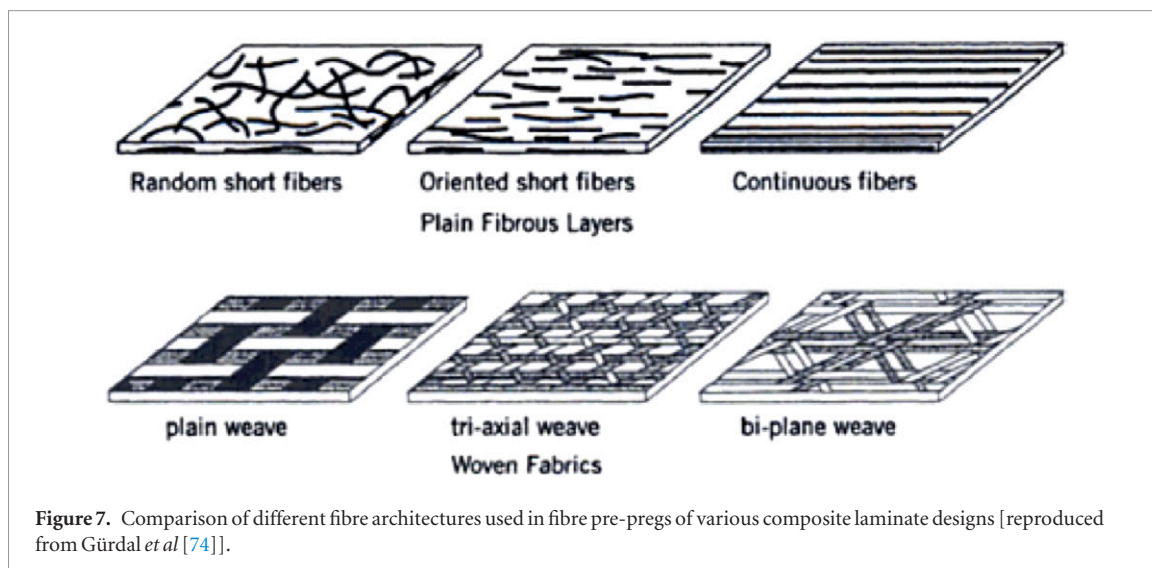


Figure 7. Comparison of different fibre architectures used in fibre pre-pregs of various composite laminate designs [reproduced from Gürdal *et al* [74]].

alterations to the materials design/configuration [74, 75].

Combined with the various potential PGF compositions and their associated mechanical properties (section 2.4), various degradable polymers have been investigated as the matrix phase. These include polylactic acid (PLA), polyglycolide (PGA), polycaprolactone (PCL) as well as polyhydroxybutyrate-co-valerate (PHB-V). Yet despite the various polymers available, most dense biomedical PGF composites for fracture fixation plates have used PLA or PCL as the matrix phase [6, 32, 55, 76]. These typically have been manufactured from a manual lay-up, film stacking process where polymer matrix sheets are stacked alternatively between layers of fibre lamina. These lamina are constructed of either isolated fibres or as pre-coated fibre impregnated sheets (known as pre-pregs). Such pre-pregs can be formed by solvent casting PGF batches with a low viscosity polymer solution and aim to enhance matrix infiltration into the fibre lamina to improve the quality of the fibre-matrix interface.

Furthermore by altering the reinforcing phase distribution (i.e. geometrical orientations) composites with isotropic or anisotropic properties can be produced using discontinuous or continuous PGF phases. However with the use of continuous reinforcing phases, the mechanical properties of PGF composites can be further modified through specific fibre orientations of each fibre lamina (e.g. 0° , 45° , 90°) or 2D fibre weaves (figure 7) [74]. Consequently implant materials with tailorable mechanical properties, designed for the mechanical loading regime of a specific anatomical site can be created through specific composite constructs relating to these material variables [15, 74].

3.2. Composite investigations

Composites of $0.06 V_f$ and $0.18 V_f$ were investigated by Ahmed *et al* [32] using as-prepared and annealed binary $(P_2O_5)_{50}-(CaO)_{50}$ (mol%) chopped 10 mm fibres that were randomly dispersed within a PCL matrix. Mechanical testing showed no improvements

to the flexural strength (σ_{comp}) from the introduction of as prepared PGFs, but an increase in the elastic modulus (E_{comp}) from 0.5 GPa to 2.4 GPa was observed for $0.18 V_f$ PCL composites that was deemed to be within the range for trabecular bone. However, the use of annealed fibres produced increases to both the initial flexural strengths and elastic moduli of the resulting composites for the same fibre volume fraction [32].

The subsequent degradation of these composites in deionised water at $37^\circ C$ over five weeks found that decreases to the sample weight and media pH (≈ 4) occurred upon the immersion of both as-prepared and annealed fibre composites. Compared to PCL controls, this weight loss was attributed solely to the dissolution of the reinforcing fibres (figure 8) with a plateau in the weight loss after ≈ 2 weeks signalling complete dissolution of the fibres (figure 9). This plateau correlated with changes to the ionic concentrations of the degradation media from the release of the glass fibres constituent ions as they degraded. The release of phosphate species ($P_2O_7^{4-}$, $P_3O_{10}^{5-}$ etc.) during fibre dissolution and the formation of phosphoric acid also accounted for the decrease in media pH over the initial 2 weeks. These results were subsequently considered to highlight how surface area effects dominated the composite degradation behaviour [32].

Further studies on the fracture behaviour and *in vitro* response of a reinforced organic methacrylate modified oligolactide composite was assessed by Brauer *et al* [77] using $125 \mu m$ diameter polyphosphate $(P_2O_5)_{35}-(CaO)_{27.5}-(MgO)_{9.5}-(Na_2O)_{22.5}-(TiO_2)_{5.5}$ (mol%) fibres. The resulting unidirectionally (UD) aligned fibre composites were found to possess flexural strengths of 115.4 ± 11.9 MPa and elastic moduli of 16 ± 2.4 GPa. These were deemed to be within those for cortical bone whilst the mechanical testing data showed the composites to fail in a fibrous fracture mode that was regarded as desirable for biomedical implants. Meanwhile the culturing of composite samples with murine MC3T3-E1 cells demonstrated their biocompatibility. However SEM imaging at the composite frac-

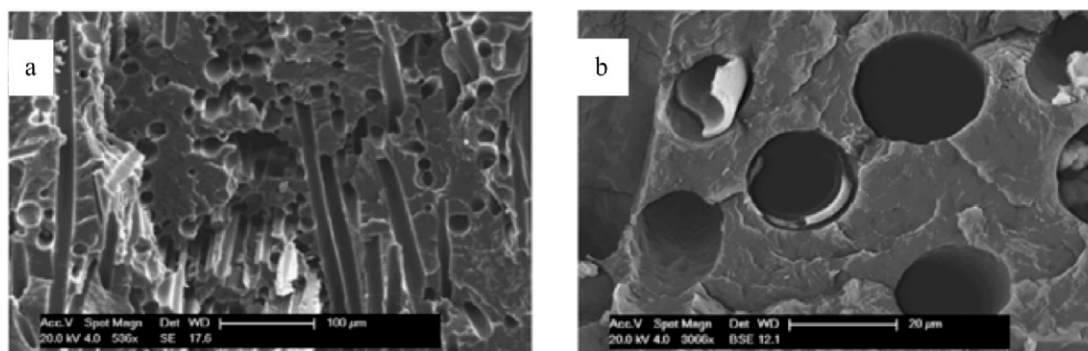


Figure 8. SEM images of (a) 0.17 V_f -PCL composite samples using as-prepared fibres after 840 h of immersion showing the porous interior created from dissolution and (b) fracture surface of a 0.18 V_f -PCL composite sample using annealed fibres after 5 weeks in deionised water at 37 °C [reproduced from Ahmed *et al* [32]].

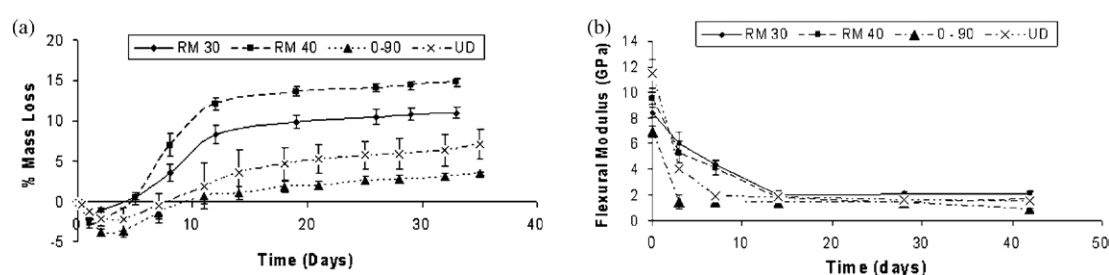


Figure 9. Comparison of (a) sample weight loss (%) and (b) elastic modulus during the degradation of different sample configurations over a 4.5 week period in deionised water at 37 °C for 30 and 40 vol% randomly orientated chopped 10 mm fibre mats (RM 30 and RM40) (0-90) cross-ply and unidirectional (UD) architectures [reproduced from Ahmed *et al* [76]].

ture sites also showed evidence of sample delamination that indicated poor interlaminar bonding [77].

The retention of mechanical properties and biocompatibility of PGF-PLA composites was examined by Ahmed *et al* [41] who characterised samples using a $(P_2O_5)_{50}-(CaO)_{40}-(Na_2O)_5-(Fe_2O_3)_5$ (mol%) composition of as-prepared and annealed $\phi = 20-25 \mu m$ fibres. These composites were generated by incorporating chopped, randomly orientated 10 mm non-woven fibres into a PLA matrix at a 0.14 fibre volume fraction (V_f) using a manual lay-up, film stacking technique. As expected, the inclusion of PGFs increased the elastic modulus and flexural strength of the non-reinforced PLA from 2.5 to 5 GPa and 50 to 90 MPa respectively. In contrast to earlier studies by Ahmed *et al* [32], a comparison between the mechanical properties of equivalent composites using as-prepared and annealed fibres found the differences not to be statistically significant.

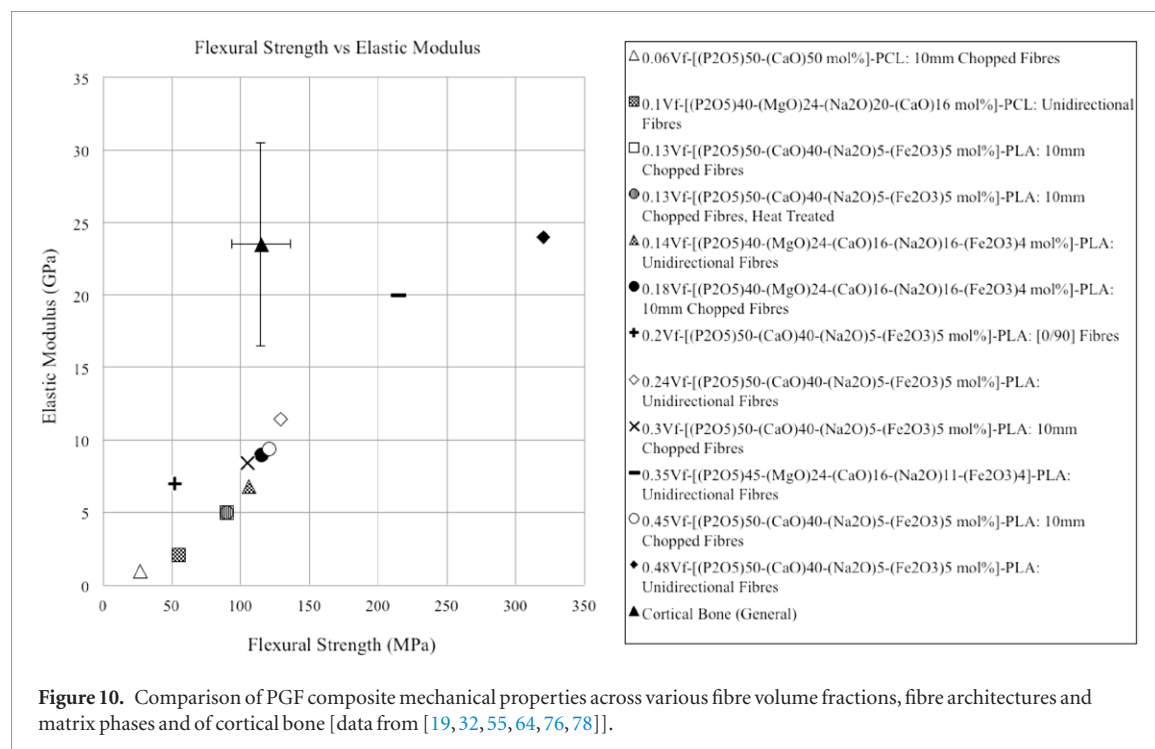
As previously seen with the PGF-PCL composites investigated by Ahmed *et al* [32], an initial weight loss and plateau after ≈ 2.5 weeks was observed during degradation of these composites in deionised water at 37 °C for up to 6.5 weeks. This was coupled with a decrease in the media pH (< 4) over the first 2 d due to the formation of phosphoric acid (H_3PO_4) in the degradation media. Mechanical testing also found that

the composites flexural strength and elastic modulus was reduced to 40 MPa and 1 GPa respectively after 6.5 weeks. Compared to the as-prepared fibre composites, the use of annealed fibres showed a delayed weight loss that did not occur until after 8 d immersion and then plateaued after 23 d. This correlated with a delayed drop in pH whilst the elastic modulus was also found to drop to 0.5 GPa after 6.5 weeks of degradation [41]. Such results were attributed to a decreased fibre D_r produced by the annealing process, as found in previous studies of isolated fibres [24, 45, 54]. This reduction in fibre D_r was also considered to be responsible for the improved biocompatibility found from the use of annealed fibres when composite samples were cultured with MG63 cells. However despite the good biocompatibility of the samples, these composites were unable to match the elastic modulus of cortical bone or to retain adequate mechanical properties during degradation [41].

Khan *et al* [78] investigated PGF-PLA composites, using 3-aminopropyl triethoxy silane (APS) treated $(P_2O_5)_{40}-(MgO)_{24}-(CaO)_{16}-(Na_2O)_{20}$ (mol%) fibres, manufactured through either *in situ* polymerisation or compression moulding. Unidirectionally orientated fibre composites were manufactured at 0.25 V_f (*in situ* polymerised) and 0.1 V_f (compression moulded) after treating the fibres with a 1 v/v APS

Table 3. Comparison of composite mechanical properties for different fibre volume fractions (V_f) and fibre architectures (data estimated from Ahmed *et al* (2011) [76]).

Composite design	V_f	Flexural strength (MPa)	Elastic modulus (GPa)
10 mm discontinuous random	0.2	80	5
10 mm discontinuous random	0.3	105	8.4
10 mm discontinuous random	0.4	121	9.4
Continuous [0°/90°] cross-ply	0.2	52	7
Continuous unidirectional	0.2	129	11.5



solution. As expected, the higher volume fraction samples possessed an increased flexural strength ($\sigma_{\text{comp}} = 105 \pm 12$ MPa) and elastic modulus ($E_{\text{comp}} = 5.9 \pm 0.4$ GPa) compared to the 0.1 V_f compression moulded samples ($\sigma_{\text{comp}} = 55 \pm 8$ MPa, $E_{\text{comp}} = 2.1 \pm 0.3$ GPa). This was coupled with improved impact strengths (IS) and hardness with the *in situ* polymerised samples (IS = 27 ± 4 kJ m⁻², hardness = 93 ± 0.6) compared to the compression moulded samples (IS = 14 ± 3 kJ m⁻², hardness = 90.5 ± 0.4) [78]. The degradation of these samples in deionised water at 37 °C showed that the decrease in mechanical properties varied between the manufacturing techniques. The *in situ* composites retained 86.6% and 83.1% of their flexural strength and elastic modulus respectively after six weeks of degradation, compared to 43.6% (σ_{comp}) and 52.4% (E_{comp}) retained by the compression moulded composites which was attributed to the weaker fibre-matrix interface created using the compression moulding technique [78].

Meanwhile a comparison between different composite fibre architectures and volume fractions using a (P₂O₅)₅₀–(CaO)₄₀–(Na₂O)₅–(Fe₂O₃)₅ (mol%) PGF composition was performed by Ahmed *et al* [76] with the aim of producing samples with mechanical proper-

ties closer to those of cortical bone. Composites of 0.2 V_f , 0.3 V_f and 0.4 V_f were produced from randomly orientated chopped 10 mm fibre mats as well as unidirectional (UD) and [0/90] cross-ply architectures at 0.2 V_f by compression moulding. Mechanical testing showed the expected increases in flexural strength and elastic moduli with increasing fibre volume fraction that were predicted by the ‘rule of mixtures’ [76]. A comparison across different fibre architectures at 0.2 V_f also showed the mechanical properties of the [0/90] composites to be lower than the UD samples (table 3). This was due to the stress loads being axially distributed along all the fibre lengths in the UD composites with regards to the loading axis used during mechanical testing [76].

The immersion of the composites in deionised water 37 °C showed reductions in mechanical properties for all fibre volume fractions and fibre architectures. Accordingly, the flexural strength of the 0.3/0.4 V_f random fibre composites decreased to 40–50 MPa after two weeks of immersion with a decrease in the elastic modulus to close to the matrix values. Differences between the continuous fibre samples were also seen during degradation with rapid decreases to the flexural strength observed in the UD (40–50 MPa) and [0°/90°] (6–8 MPa) samples after 7 d immersion. These reductions in strength were cou-

pled with a decrease in the elastic modulus over the first 3 d of degradation for the UD (4 GPa) and $[0^\circ/90^\circ]$ (≈ 2 GPa) samples. The dissolution of these reinforcing fibres and loss in composite mechanical properties was coupled with pH drops in all media to 3.0 after 5 d of immersion and decreases in the sample weight which plateaued after approximately 12 d [76]. These variations in composite degradation behaviour were attributed to the different fibre configurations and the relative ease at which water could wick along the continuous fibre architectures compared to the discontinuous chopped fibres. These results consequently demonstrated the importance of fibre architecture on the initial mechanical properties and its effect on sample degradation [76].

Similarly, composite architectures were investigated by Felfel *et al* [55] using the $(\text{P}_2\text{O}_5)_{40}-(\text{MgO})_{24}-(\text{CaO})_{16}-(\text{Na}_2\text{O})_{16}-(\text{Fe}_2\text{O}_3)_4$ (mol%) fibre composition previously investigated by Haque *et al* [35] for random (10 mm chopped) and unidirectionally oriented (UD) fibre orientations at a targeted 0.18–0.2 V_f . These samples followed the expected trends with the greatest increase in flexural strength and elastic modulus recorded from the UD composites ($\sigma_{\text{comp}} = 115$ MPa, $E_{\text{comp}} = 9$ GPa) compared to randomly oriented ($\sigma_{\text{comp}} = 106$ MPa, $E_{\text{comp}} = 6.8$ GPa) and PLA control ($\sigma = 90$ MPa, $E = 3.8$ GPa). Degradation of these samples in PBS at 37 °C found that the difference in PGF composition and composite architecture resulted in different degradation behaviour. A decrease in the flexural strength of the random fibre composites was found to occur after 2 weeks degradation to 75 MPa and then 50 MPa after 13.5 weeks. However, in contrast to the results previously recorded by Ahmed *et al* [76], the flexural strength of the UD composites showed improved retention (compared to the random fibre architectures) and did not decline until after 8 d of degradation—decreasing to ≈ 75 MPa. The elastic modulus of the UD composites was also seen to increase and plateau to 10 GPa after 200 h of immersion that contrasted the random fibre composites and showed a decrease to 4.5 GPa after 2 weeks. The failure behaviour of both composite fibre architectures was also seen to evolve from an initially brittle fracture to a ductile failure mode that was due to plasticisation of the polymer phase produced by water ingress, water absorption and short fibre pull out. These results were primarily attributed to the fibres that were stated to have a D_r of 3×10^{-6} mg cm $^{-2}$ h $^{-1}$. However this composition was also stated as being difficult to manufacture whilst no clear explanation was given for the discrepancies between the fibre architectures [55].

Harper *et al* [79] compared this glass composition with the $(\text{P}_2\text{O}_5)_{50}-(\text{CaO})_{40}-(\text{Na}_2\text{O})_5-(\text{Fe}_2\text{O}_3)_5$ (mol%) composition previously studied by Ahmed *et al* [76] concentrating on the experimental mechanical properties of random 10 mm chopped PGF-PLA composites with those predicted by the rule of mixtures and FEA modelling. Comparing the experimental and

theoretical elastic moduli confirmed the accuracy of the FEA projections and allowed the model to identify composite configurations to produce samples with elastic moduli at the upper range of cortical bone (i.e. 20 GPa). From this study it was found that composite samples could not be manufactured to meet this cortical bone target range without altering the fibre length or introducing fibre alignment, this was despite theoretical changes to the fibre tensile modulus (50 to 100 GPa) or volume fraction from 0.1 to 0.5 V_f . However this study also discussed how the 10 mm fibre length (used in the majority of studies) consequently limited the practical composite volume fraction, but was suited to the aggressive mixing techniques used in composite manufacturing. The practical difficulties in aligning a discontinuous reinforcing phase was also highlighted [76, 79].

The characterisation of bulk monoliths as well as PGF-PLA and PGF-PCL composites using compositions doped with SiO_2 and Fe_2O_3 was evaluated over a range of $(\text{P}_2\text{O}_5)_{50}-(\text{CaO})_{40}-(\text{SiO}_2)_{10-x}-(\text{Fe}_2\text{O}_3)_x$ (x : 0, 5, 10 mol%) glasses [33, 68]. They studied the change in fibre solubility and surface hydrophilicity produced by the incorporation of SiO_2 due to its ability to disrupt the PG network. As seen with previous studies, the incorporation of 10 mm length, ≈ 10 – 20 μm diameter PGFs in a PLA or PCL matrix (≈ 0.18 V_f) resulted in an increase to the flexural strength and elastic modulus [33, 68]. Comparisons of degradation in distilled water or PBS revealed that the 10 mol% Fe_2O_3 composites showed a lower weight loss and greater retention of mechanical properties compared to the 5 mol% SiO_2 samples. This effect was believed to be due to the decreased D_r of the 10 mol% Fe_2O_3 PGFs compared to the 5 mol% SiO_2 composition which also produced an acidic pH (≈ 3.5) during sample dissolution [68]. However they also discussed how the increased hydrophilicity of the SiO_2 containing compositions would also influence the PGF composites dissolution during immersion. Consequently the PCL- $(\text{Fe}_2\text{O}_3)_{10}$ composites showed no statistically significant reduction in their flexural strength (≈ 40 MPa) or elastic modulus (≈ 2 GPa) after 4 weeks degradation in PBS. The difference in PGF D_r was also observed to be responsible for the precipitation of brushite ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$) on the PCL- $(\text{SiO}_2)_5$ - $(\text{Fe}_2\text{O}_3)_5$ composite surfaces when immersed in SBF due to the high ion release and acidic pH caused by the fibre dissolution compared to the PCL- $(\text{Fe}_2\text{O}_3)_{10}$ samples that showed no precipitate. Meanwhile *in vitro* cell culture studies using MC3T3-E1 preosteoblasts also found that all composite configurations demonstrated acceptable biocompatibility [33, 68].

Meanwhile Han *et al* [19] showed that an increase in the flexural strength and elastic modulus could be achieved from the use of eight fibre pre-preg mats ($\sigma_{\text{comp}} \approx 225$ MPa, $E_{\text{comp}} \approx 17$ GPa) compared to a single fibre lamina ($\sigma_{\text{comp}} \approx 125$ MPa, $E_{\text{comp}} \approx 9$ GPa) during the compression moulding of composites at 0.25 V_f . This was due to the improved polymer infiltration when using

multiple $(\text{P}_2\text{O}_5)_{50}-(\text{CaO})_{40}-(\text{Na}_2\text{O})_5-(\text{Fe}_2\text{O}_3)_5$ (mol%) fibre mats and the quality of the fibre-matrix interface. Increases in fibre volume fractions also showed that the highest mechanical properties were achieved with unidirectionally aligned 0.45 V_f samples ($\sigma_{\text{comp}} \approx 320$ MPa, $E_{\text{comp}} \approx 16$ GPa). The introduction of 2 mm screw holes reduced the flexural strength but was determined to be statistically insignificant. However, changes to the elastic modulus were found to be statistically significant after the introduction of screw holes into composites using multiple fibre mats. The choice of fibre architecture was also found to influence the damage zone incurred during the drilling process with greater damage incurred in UD fibre composites compared to random or mixed fibre constructs (i.e. UD + chopped random) [19].

The degradation of samples in PBS at 37 °C over 30 d found that all samples showed an initial increase in mass (due to water absorption) that, after 7 d, was followed by a mass loss. This was coupled with an initial decrease in pH from 7.5 to ≈ 6 after seven days of degradation which returned to neutral after fourteen days. Furthermore the 0.45 V_f composites showed the greatest rate of weight loss with the introduction of screw holes showing the same trends in weight loss and pH behaviour, however, no mechanical data was provided. Additionally, they acknowledged that despite previous studies showing that this composition of PGF would degrade too rapidly (Ahmed *et al* [32]), its ease of manufacturing made it highly suitable for investigating different composite configurations and their initial material properties. Finally, the effect of gamma sterilisation was examined due to its known ability to decrease polymer molecular weight and thus accelerate degradation. The results found that a statistically significant decrease in elastic modulus was observed after a single irradiation cycle of 36.7 Gr [19].

3.3. Composite modification

Owing to the ability of surface treatments to potentially repair fibre surface damage as well as introduce a degree of hydrophobicity at the fibre-matrix interface, PGF composites using coupling agents have been investigated to improve both the initial mechanical properties and mechanical property retention during degradation.

An examination into the effect of an APS sizing agent on the mechanical properties of PGF-PCL composites across different concentrations of APS was examined by Khan *et al* [80] using a $(\text{P}_2\text{O}_5)_{40}-(\text{MgO})_{24}-(\text{CaO})_{16}-(\text{Na}_2\text{O})_{20}$ (mol%) composition of PGF. Mechanical testing of composites with unidirectionally aligned fibres at 0.1 V_f found that the use of 5 wt% APS sizing agent increased the initial flexural strength from ≈ 52 MPa to 75 MPa and elastic modulus from 1.85 GPa to 3.1 GPa respectively, 10 wt% treated fibres further increased these properties to 79 MPa and 3.4 GPa respectively. The degradation of these composites for six weeks in deionised water at 37 °C also showed that the sizing agent improved the retention of the

mechanical properties with the 10 wt% treated composites retaining 63% and 74% of their flexural strength and elastic modulus respectively in contrast to the 54% (σ_{comp}) and 58% (E_{comp}) when as-prepared fibres in a PCL matrix were used. This was coupled with a trend of decreasing composites mass loss as the APS concentration used to treat the fibres was increased [80].

A comparison of different surface treatments on $(\text{P}_2\text{O}_5)_{45}-(\text{CaO})_{16}-(\text{MgO})_{24}-(\text{Na}_2\text{O})_{11}-(\text{Fe}_2\text{O}_3)_4$ (mol%) unidirectionally aligned fibres in a PLA matrix (0.35 V_f) was performed by Hasan *et al* [69] for three different coupling agents. These coupling agents were 3-aminopropyltriethoxy silane (APS), hexamethylene diisocyanate (HDI) and sorbital ended PLA oligomers (SPLA) with the mechanical properties before and after 4 weeks immersion in PBS at 37 °C measured. Statistically significant increases in the initial flexural strength from 215 MPa to 300 MPa (APS) or 260 MPa (SPLA) were obtained. Yet only SPLA produced statistically significant increases in the elastic moduli from 20 to 25 GPa. However these increases to the initial mechanical properties did not directly correlate with increased mechanical property retention. No statistically significant differences were found between the different surface treatments on the resulting elastic moduli after 28 d of degradation. The culture of primary human osteoblasts on these samples found no cytotoxic effects from the use of these surface treatments [69].

Continuing from their previous studies, Liu *et al* [81] examined the use of Mg coated 10 mm chopped, randomly orientated, $(\text{P}_2\text{O}_5)_{45}-(\text{CaO})_{16}-(\text{MgO})_{24}-(\text{Na}_2\text{O})_{11}-(\text{Fe}_2\text{O}_3)_4$ (mol%) fibres in a PCL matrix at 0.2 V_f after the deposition of a 2 μm thick Mg coating. The incorporation of non-coated fibres raised the flexural strength from ≈ 20.0 to 33.6 MPa and the elastic modulus from 0.4 to 2.2 GPa. However, any further change in mechanical properties of the composites from the Mg coating of fibres were found to be statistically insignificant ($\sigma_{\text{comp}} = 37.0$ MPa, $E_{\text{comp}} = 2.4$ GPa) compared to the non-coated fibre composite [81]. The degradation of these samples in PBS at 37 °C showed the flexural strength of the non-coated fibre composites to decrease and plateau at 22.8 MPa after 24 h of degradation with the Mg-coated fibre composites reducing to 28.9 MPa over the same period. Correlating with this was the reduction in elastic modulus for non-coated and Mg-coated fibre composites to 0.9 GPa and 2.1 GPa respectively. After ten days these moduli were seen to further reduce to 0.6 GPa (non-coated) and 1.5 GPa (Mg-coated). The weight loss data also showed that the application of an Mg coating inhibited degradation of the fibre-matrix interface with a reduced weight loss for the Mg-coated samples (0.2%) compared to the non-coated fibres (3%) after ten days of degradation. Biocompatibility testing of these samples using MG63 cells for up to 14 d showed no significant differences between the different composite samples with regards to the metabolic activity or differentiation with similar cell morphologies observed on all samples [81].

Finally alternative treatments aimed at addressing the drop in pH and autocatalytic effects through the incorporation of a secondary chemically basic calcium carbonate (CaCO_3) phase into a methacrylate-modified matrix were investigated by Kobayashi *et al* [57] for an ultraphosphate (P_2O_5)_{51.04}–(CaO)_{21.42}–(Na_2O)_{25.51}–(SiO_2)_{2.03} PGF composite. The development of these fibre-particle hybrid composites subsequently showed that the incorporation of 20 wt% CaCO_3 led to a transition in the failure behaviour of these samples from a ductile, fibrous failure to a brittle fracture mode. Mechanical testing also found that both fibre only and fibre-particle composites had elastic moduli ranging from 15 to 20 GPa. The immersion of samples over ten days in NaCl solution at 37 °C also showed that the CaCO_3 was successful at reducing the pH drop, produced by the dissolution of the reinforcing PGFs, from 2.0 to 4.6 [57].

3.4. Discussion on PGF composites

As studies on PGF composites have shown, the use of conventional concepts on engineering composite design have been used to try and develop materials with mechanical properties matching those of cortical bone. As such, the studies examined here have investigated a variety of factors related to PGF composite design that have included the PGF composition, matrix material, fibre architecture and more novel sample configurations. Yet despite the range of composite mechanical properties found in these materials [19, 32, 76, 78], few samples have managed to reach those of cortical bone (figure 10), although this may be due to the relatively low volume fraction of fibres typically used in these materials (≈ 0.1 – $0.2 V_f$). Yet the results here have also highlighted the inability of current PGF composites to maintain these mechanical properties over a prolonged duration once immersed in media despite the different composite designs or post-processing (i.e. annealing of the reinforcing fibres). This has been due to the high surface area-to-volume ratios at the fibre-matrix interface and the autocatalytic effects on PGF D_r that can be detrimental to the mechanical integrity and biocompatibility of the composites. Accordingly, as the results of Ahmed *et al* [76] have shown, the increases in V_f required to achieve composites with mechanical properties closer to those of cortical bone will further accelerate the rate of fibre dissolution due to the increased release of phosphate species into the media [76].

With regards to the rapid decreases in composite mechanical properties, the results of these various studies also emphasise the need for composite design to consider how the material configuration can influence both the initial and subsequent degenerative mechanical properties. This is evident by the increased mechanical properties obtained from a continuously aligned fibre-reinforcing phase being offset by the accelerated rate at which moisture can wick along the fibre-matrix interface compared to the use of a mechanically weaker,

randomly orientated discontinuous phase (Ahmed *et al* [76]). Furthermore studies by Han *et al* [19] illustrate the additional considerations that must be given to how the composite configuration can influence the workability of these materials in practical application (e.g. the incorporation of screw holes for implant fixation) [19, 76].

With regards to these issues, it is apparent that the development of more durable PGF compositions (i.e. reduced D_r) would be a logical route to improving PGF composite durability. As such, the continued investigation of PGF manufacturing from reduced P_2O_5 compositions (such as those studied by Sharmin *et al* [24]) could be advantageous for developing composites with improved durability. Furthermore given that modifications to the fibre-matrix interface via the use of coupling agents (Khan *et al* [80]) have so far failed to adequately improve composite mechanical property retention—it would appear that modifications to the PGF composition should take precedent. Accordingly it would seem that surface modifications through the use of more novel surface treatments (such as the Mg coated PGF in PCL composites investigated by Liu *et al* [81]) would be beneficial if applied in tandem with improved PGF compositions.

However the use of a secondary chemically basic calcium phosphate phase may be an effective method for counteracting these autocatalytic effects and enhancing PGF composite durability, as initially investigated by Kobayashi *et al* [57]. Given that conventional engineering fibre-particle hybrid composites are considered by Fu *et al* [82] as being capable of possessing good fracture toughness and impact strengths, such PGF materials may be useful for further tailoring the composites mechanical properties whilst reducing the PGF D_r . Furthermore the development of more novel matrix materials is another design route that may also be beneficial to maintaining the mechanical properties of the composite materials. This is due to the acidic degradation by-products released from the degradation of PLA that would also be likely to compromise the fibre-matrix interface during sample degradation.

Yet besides these variables, other avenues related to the composite manufacturing may also be advantageous for improving material performance. This relates to the improved mechanical properties found from the use of *in situ* polymerisation techniques by Khan *et al* [78] compared to compression moulding methods commonly used throughout these studies. Furthermore the development of discontinuously aligned chopped fibre composites (as discussed by Harper *et al* [79]) would also seem an attractive option for increasing composite mechanical properties whilst inhibiting wicking along the fibre-matrix interface.

However the potential use of low D_r PGF as a single reinforcing phase would also appear to be counter active to the potential benefits of these PGF materials (as discussed in the Introduction) due to the subsequent reduction in the ions released from the composites.

This would subsequently reduce the osteoinductivity or other potential stimulatory/therapeutic effects that PGFs could evoke (e.g. anti-bacterial responses). However as discussed by Mohammadi *et al* [68], the PGF D_r and rate at which these ions released will also influence the bioactivity of these composites and the precipitated calcium phosphate phase. As a result, future PGF composites wishing to incorporate such stimulatory features whilst retaining suitable mechanical properties during sample degradation may require the combination of multiple PGF phases using low and high D_r PGF phases. These could then work in tandem to simultaneously provide mechanical reinforcement and *in vivo* stimulus.

3.5. Conclusions

Due to their tailorable properties PGFs are an attractive option to reinforce biomedical composites with a variety of investigations aimed at developing PGFs with reduced dissolution rates and increased mechanical properties. These studies have subsequently resulted in the development of ultra- (>50 mol% P_2O_5), meta- (50 mol% P_2O_5) and polyphosphate (<50 mol% P_2O_5) PGF compositions with a range of mechanical properties. They have the potential to exhibit tensile moduli close to those of commercially available glass fibres such as S-Glass or E-Glass. However so far the PGFs investigated remain susceptible to autocatalytic effects due to the large surface area to volume ratios and acidic dissolution by-products despite variations in the glass composition and post fibre processing (e.g. annealing or via coupling agents). Furthermore, these studies have highlighted that despite the perceived versatility of PGF materials, the potential for compositional variability is limited by the need to develop biocompatible fibres with high mechanical properties and low dissolution rates that can also be easily manufactured into continuous fibres (typically represented by their thermal stability described by the compositions processing window). However the use of intermediate oxides and other compositional arrangements such as those aimed at better regulating the dissolution media pH appear promising for the development of PGF reinforcing phases.

Based on engineering composite theories, the incorporation of PGFs into various degradable polymer matrices has led to a range of mechanical properties for different composite configurations that are within the range of cortical bone. However these materials appear to retain inadequately these mechanical properties during sample degradation, that is, to retain at least 80% of these properties after six to eight weeks of degradation (Pietrzak and Eppley [25]). As with the isolated PGF samples, this rapid loss in mechanical properties has been attributed to the ingress of moisture and rapid breakdown of the fibre matrix interface due to the high surface area-to-volume ratios at the fibre-matrix interface and wicking of fluid into this interface. Yet it is also evident that the application of composite theory to PGF composite designs must also consider the apparent trade-off that exists between the initial and degenerated

mechanical properties of the samples. This is evident by the increased mechanical properties found from increases to the composite V_f or from the use of continuous fibre architectures being offset by the increased rate of mechanical property depreciation. Consequently the need for PGF composites with mechanical properties closer to those of cortical bone appears to be counter intuitive to maintaining composite durability using current philosophies and production methods.

As a result, current discussions on PGF and PGF-composites are exploring the use of alternate PGF compositions, composite designs and manufacturing techniques as well as novel fibre surface treatments in order to simultaneously improve the initial and degenerative mechanical properties of PGF composites. However given the focus on developing more durable PGF compositions (D_r), consideration should also be given to how to this could impact the potential *in vivo* bioactivity and osteoinductive properties of the resulting composites.

Acknowledgments

RC was funded by an EPSRC Scottish CASE studentship (grant number 09001298/EP/H501231) with additional funding from Giltech, Ayr, Scotland.

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